

FIG. 1

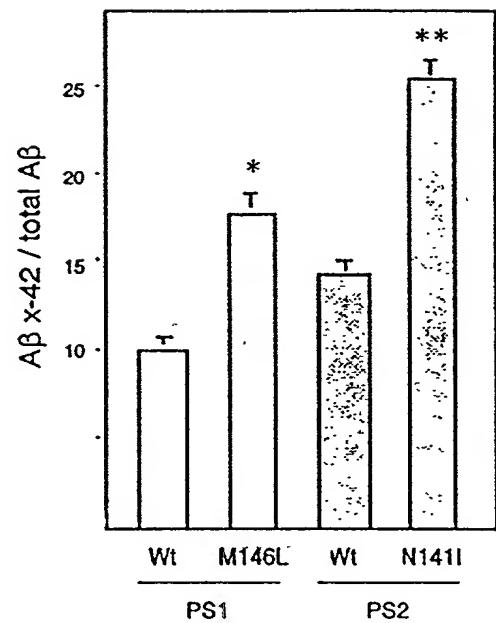


FIG. 2

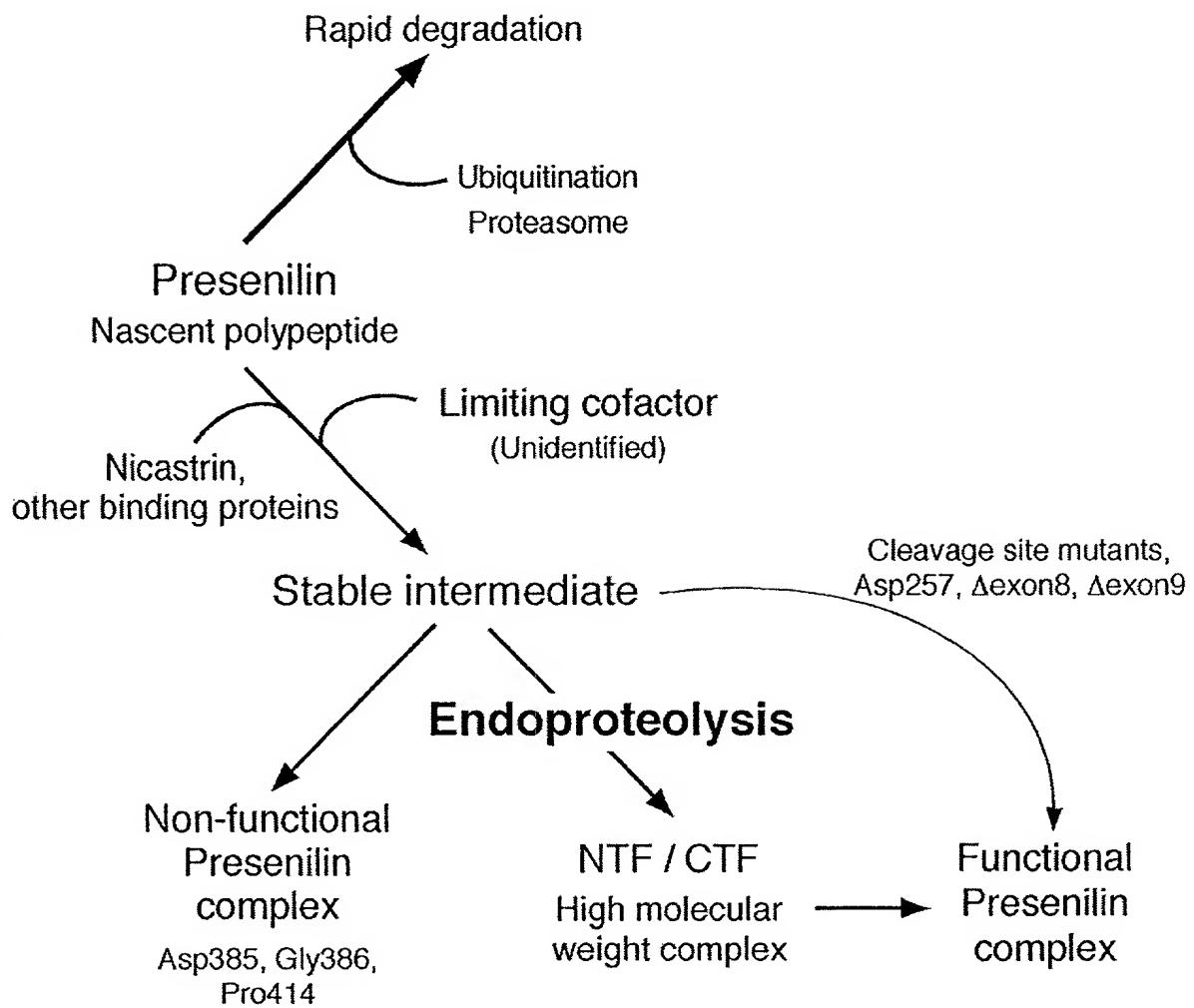


FIG. 3

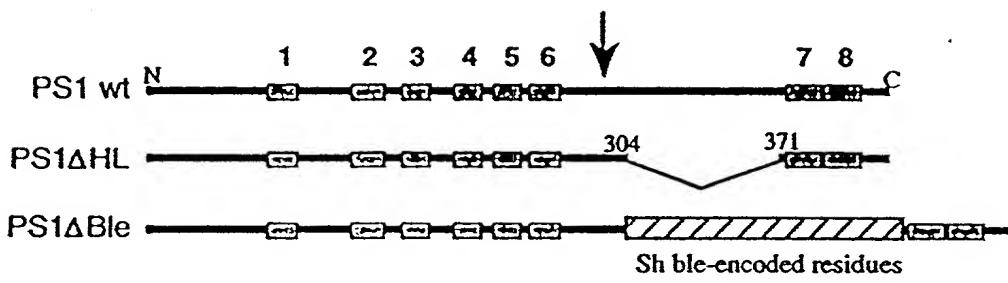


FIG. 4

TM

Hu PS1	WTAWLILAVISVYDLVAVLCPKGPLRMLVETAQERNETLFPA	LIYSSTMVVLVNMAEGDPE	AQ
Xen PS α	WTTELILAVISVYDLVAVLSPKGPLRMLVETAQERNETLFPA	LIYSSTMIWLVNMAADGDP	GL
Fish PS1	WTAWLILAVISVYDLVAVLCPKGPLRILVETAQERNEP	IFPA	P
Hu PS2	NSAVVILGAISVYDLVAVLCPKGPLRMLVETAQERNEP	IFPA	ADSAE
Xen PS β	NSAVVILGAISVYDLVAVLCPKGPLRMLVETAQERNEP	IFPA	SSAMMRTVGMAKLDP
Dros PS1	WTAWAVLAI	S	A
SEL-12	WTVFVLFVISVWDLVAVLTPKGPLRY	V	VTAVENTTDP--REP
HOP-1	WTVWALTAISFWDIVAVLTPCGPLKMLVETANRRGDDKFP	AI	LYNSSS--YNEVDSPD
consensus	Wt WLiLa ISvyDlvAVL PKGPLrmLVETaQeRne	1FPAlIYss	mvw v m

Hu PS1	RRVSKNSKYN	NAESTERESQ	-DTVA-	ENDDG	-GFSE
Xen PS α	KQSASTKTY	NTQAPTAH	PRSDSAA	SDDNG	-GFDT
Fish PS1	RNNSSH	PV	PQQENQDAVAP	PEDDG	-GFTP
Hu PS2	-----	SS	-Q	GALQL	-PYDP
Xen PS β	-----	TA	-D	GRMNQ	-QVQ-
Dros PS1	SSSNSTTT	TRATQNSLAS	SPEAAAASQRTGNSHPRQNQRDDGSV	IATEGMPLVTFKSNLRGNAEAAGFTQ	
SEL-12	TSSDSNTSTA	FPGEASC	SSETPKR	PKVKR	-IPQKV
HOP-1	-----	T	-	RSNS	-TP
consensus	e		s		

TM

Hu PS1	EWEAQ	RDHS	LGP	HRSTPESRAA	VQELSSS	-ILAGED	DPE	ERGV	KLGLGDF	FIFY	SVLVGKASAT					
Xen PS α	TWED	DHR	RNAQ	IGPINSTPESRVA	VQALPSN	-SPP	SED	PE	ERGV	KLGLGDF	FIFY	SVLVGKASAT				
Fish PS1	AWVN	QO	HQLG	PQM	IQELPS	SAR	PPP	V	DE	ERGV	KLGLGDF	FIFY	SVLVGKASAT			
Hu PS2	EMBEDSY	DSF	GEPSY	PEVFEP	LTGYPGE	--E	LE	E	ERGV	KLGLGDF	FIFY	SVLVGKA	AT			
Xen PS β	HICRNT	PEG	ANS	-TVEDAAETR	IQTQSNL	--S	SE	CD	DE	ERGV	KLGLGDF	FIFY	SVLVGKA	AT		
Dros PS1	EWSANL	SER	VARR	QIEVQSTQSGNA	SSE	CP	DE	ERGV	KLGLGDF	FIFY	SVLVGKASSY					
SEL-12	QIES	TTA	STTQNSG	VRVERELAA	ERPTVQ	DAN	FHR	HEE	ERGV	KLGLGDF	FIFY	SVLVGKASSY				
HOP-1	LT	PFN	SSSSRL	LESDSLRRPP	VI	PRQ	--I	REV	RE	V	FGT	IPLG	MGDF	VFS	SLMLGNTVQ	t
consensus	e				e											t

FIG. 5

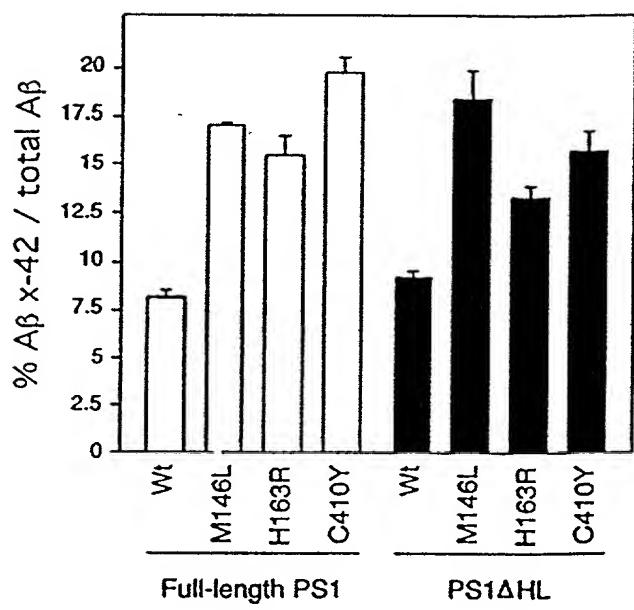


FIG. 6

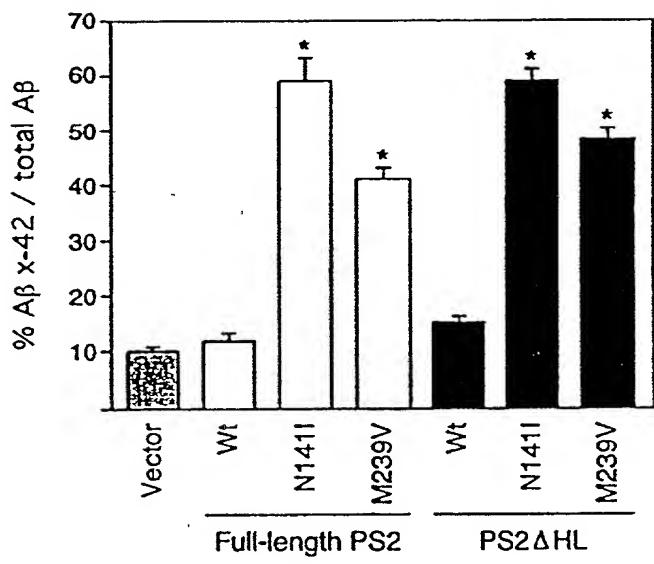
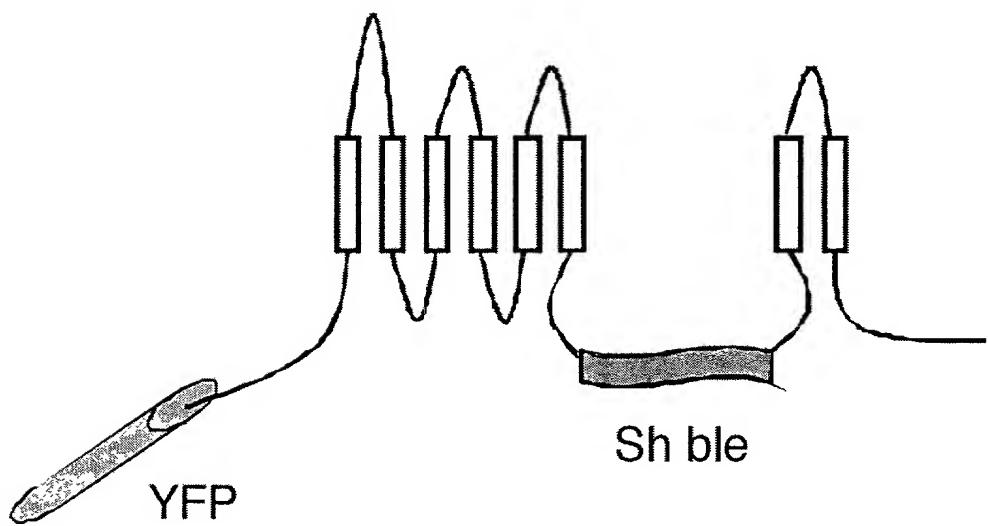


FIG. 7

PS1 chimera



Sh ble - protect from zeocin-mediated cell death

YFP - visualization

FIG. 8

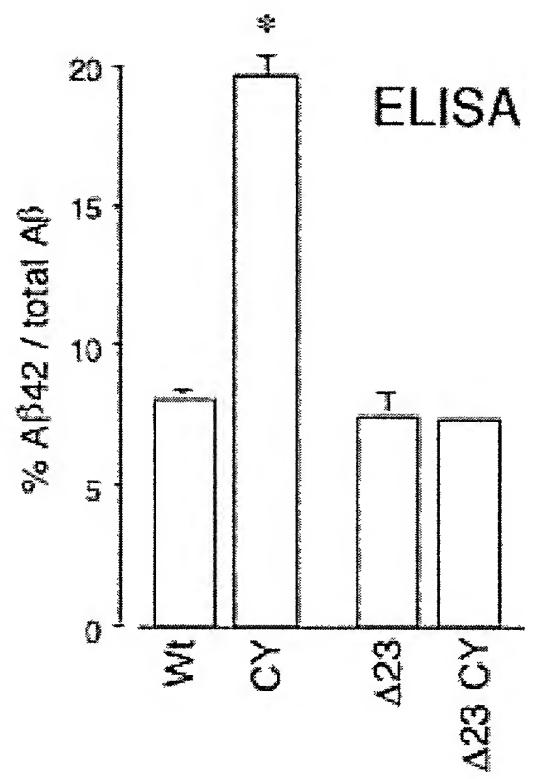


FIG. 9

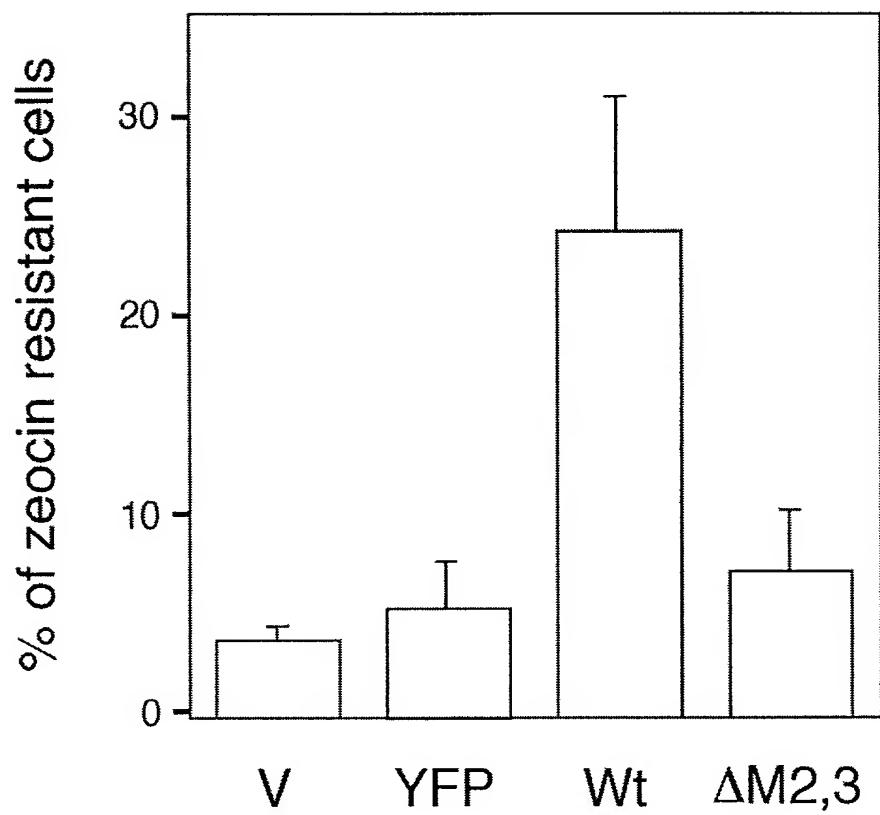
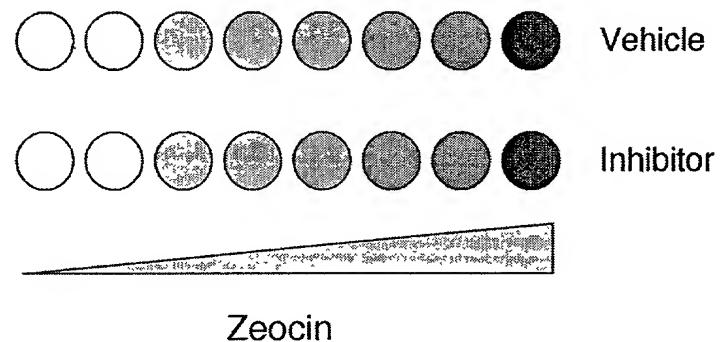


FIG. 10

Assay

Culture stable N2a cells expressing PS1 chimera in 96 well dish



Perform cell viability assay 2-3 days later

Expectation - inhibitors that affect PS1-Sh ble levels will reduce cell viability

FIG. 11

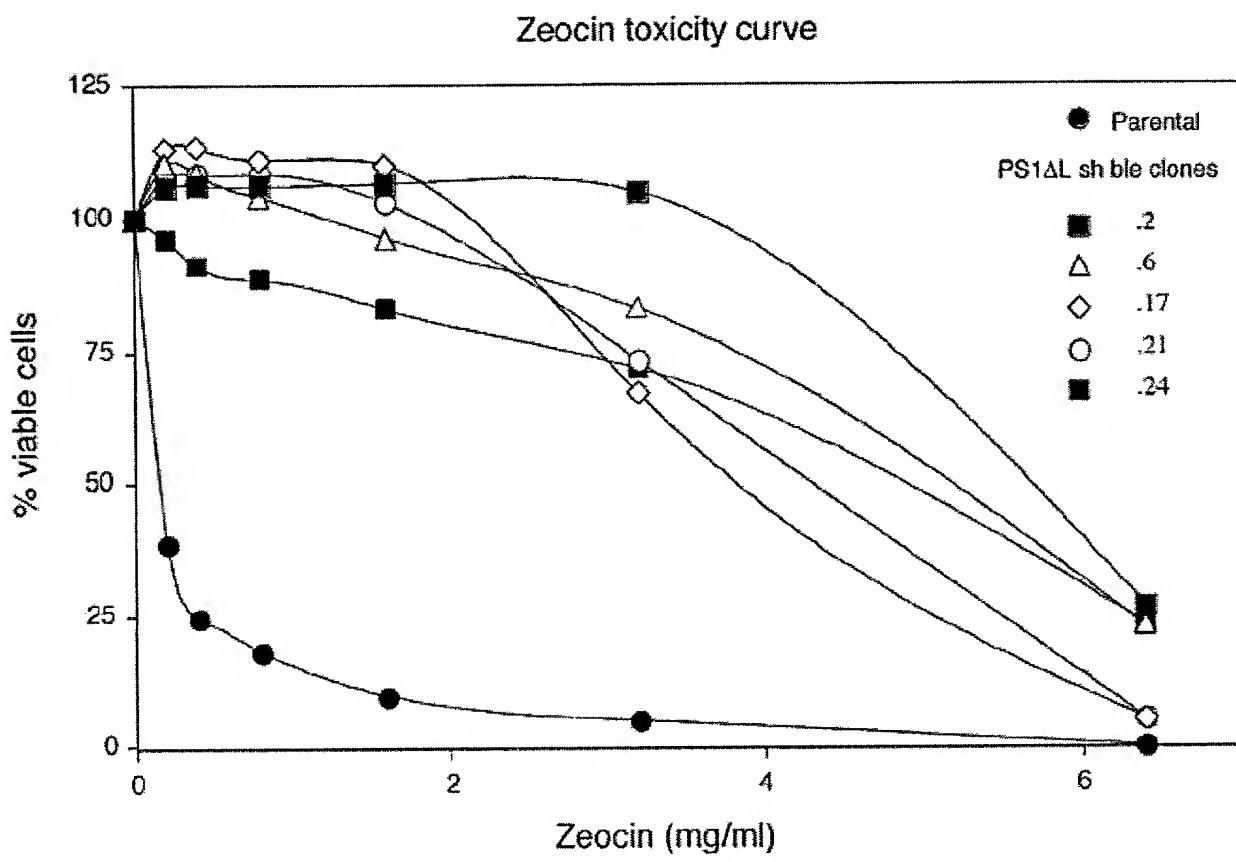


FIG. 12

Treatment with L-685,458
reduces resistance conferred by PS1 chimera

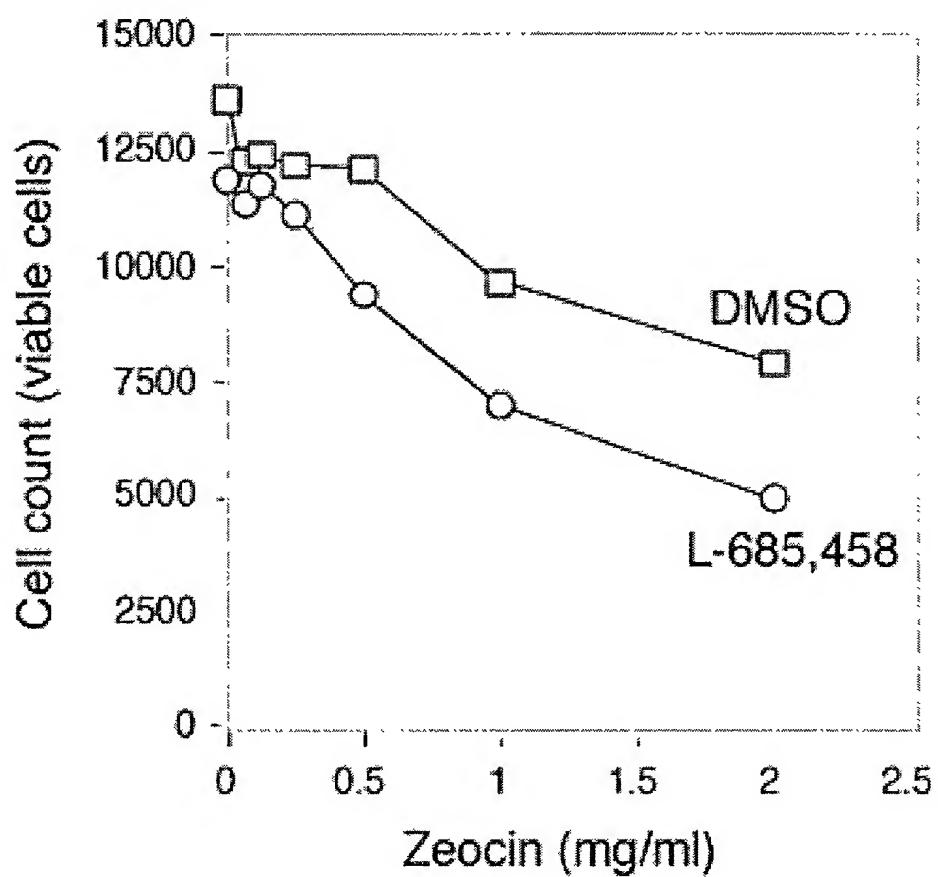


FIG. 13

Functional cloning strategy

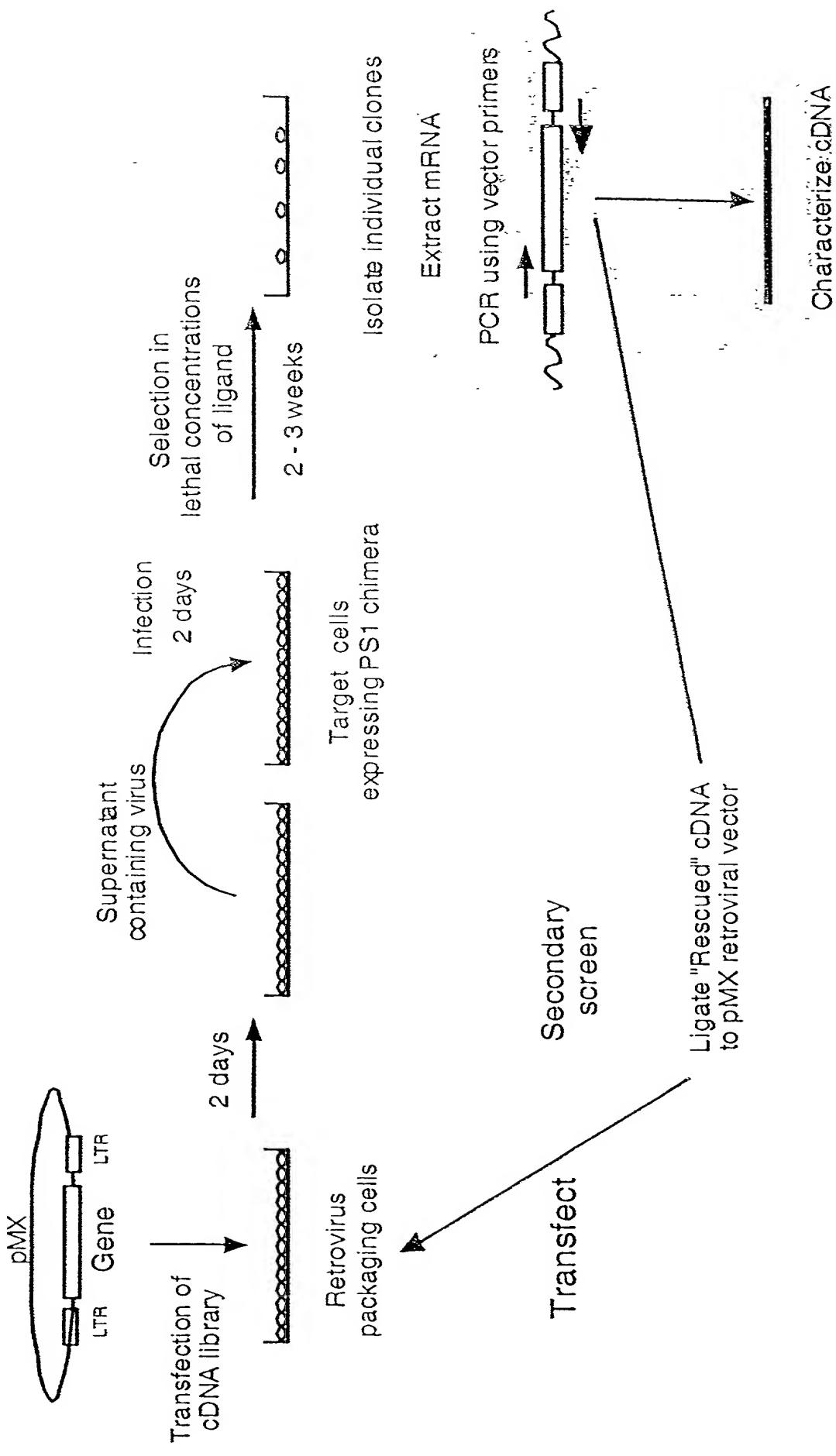


FIG. 14